

What is claimed is:

1. A method for determining the presence or absence of at least one genetic alteration in a target nucleic acid for the diagnosis and management of malignant disease, comprising:
  - a) providing a target nucleic acid from a patient sample, said target nucleic acid having a predetermined sequence in the normal population;
  - b) assessing said target nucleic acid for the extent of loss of heterozygosity relative to predetermined loci, increased loss of heterozygosity, being correlated with enhanced tumor invasiveness and metastasis.
- 10 2. The method as claimed in claim 1, wherein said genetic alteration is selected from the group consisting of inversion, deletion, duplication, and insertion of at least one nucleotide in said sequence.
- 15 3. The method of claim 1, wherein said target nucleic acid is assessed for genetic alterations via a method selected from the group consisting of restriction enzyme mapping, hybridization of allele specific probes, oligomer ligation, DNA sequencing and quantitative PCR.
- 20 4. The method as claimed in claim 1, wherein said malignancy is neuroblastoma and said genetic alteration is a single copy loss of a single nucleotide polymorphism at the 1p36.3 region of chromosome 1, said loss being associated with increased metastasis and poor prognosis.
- 25 5. The method as claimed in claim 4, wherein said Loss of heterozygosity occurs on chromosome 1 and said single nucleotide polymorphism comprises at least one of the single nucleotide polymorphisms set forth in Figure 12.
- 30 6. A method for determining the presence or absence of at least one specific nucleotide in a target nucleic acid for the diagnosis and management of malignant disease, the method comprising the steps of:
  - (a) providing a detectable amount of a target nucleic acid

polymer isolated from a chromosomal region known to be associated with malignancy in a single stranded form,

(b) hybridizing the detectable amount of the nucleic acid polymer with one or more oligonucleotide primers, wherein each primer has a nucleotide sequence that is complementary to a sequence in the target nucleic acid polymer, such that when the primer is hybridized to the target nucleic acid polymer, the 3' end of the primer binds to a nucleotide flanking the specific nucleotide at the defined site in the target nucleic acid,

(c) exposing the hybridized nucleic acid polymer to a polymerization agent in a mixture containing at least one deoxynucleotide, said deoxynucleotide comprising a detectable label, and one or more chain terminating nucleotide analogues, such that a detectable primer extension product is formed if the labeled deoxynucleotide is complementary to the specific nucleotide at the defined site;

(d) analyzing the polymerization mixture of step (c) for the presence or absence of the primer extension product containing the labeled deoxynucleotide at the 3' end thereof, whereby the identity of the specific nucleotide at the defined site is determined; and

(e) assessing said target nucleic acid for loss of heterozygosity at said at least one single nucleotide loci, the degree of loss of heterozygosity being correlatable with increased tumor invasiveness and poor patient prognosis.

7. The method of claim 6, wherein said target nucleic acid of step e) is compared to the chromosomal region of step b) which lacks genetic alterations associated with cancer.

8. The method as claimed in claim 6, wherein said malignancy is neuroblastoma and said genetic alteration is a single copy loss of a single nucleotide polymorphism at the 1p36.3 region of chromosome 1, said loss being associated with increased metastasis and poor prognosis.